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NOTICE OF ALLOWANCE AND FEE(S) DUE

27123

7590

05/03/2010

MORGAN & FINNEGAN Transition Team
C/O Locke Lord Bissell & Liddell
3 WORLD FINANCIAL CENTER
NEW YORK, NY 10281-2101

EXAMINER

POPA, ILEANA

ART UNIT

PAPER NUMBER

1633

DATE MAILED: 05/03/2010

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|------------------------------|------------------|
| 10/500,173 | 06/24/2004 | Katsuhito Takahashi | 1004331.019US (4439-4022) | 3299 |
| TITLE OF INVENTION: CELL-SPECIFIC EXPRESSION/REPLICATION VECTOR | | | | |

| APPLN. TYPE | SMALL ENTITY | ISSUE FEE DUE | PUBLICATION FEE DUE | PREV. PAID ISSUE FEE | TOTAL FEE(S) DUE | DATE DUE |
|----------------|--------------|---------------|---------------------|----------------------|------------------|------------|
| nonprovisional | NO | \$1510 | \$300 | \$0 | \$1810 | 08/03/2010 |

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. **PROSECUTION ON THE MERITS IS CLOSED.** THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN **THREE MONTHS** FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. **THIS STATUTORY PERIOD CANNOT BE EXTENDED.** SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
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 or Fax **(571)-273-2885**

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

27/123 7590 05/03/2010

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C/O Locke Lord Bissell & Liddell
3 WORLD FINANCIAL CENTER
NEW YORK, NY 10281-2101

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

| |
|--------------------|
| (Depositor's name) |
| (Signature) |
| (Date) |

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| EXAMINER | ART UNIT | CLASS-SUBCLASS |
|--------------|----------|----------------|
| POPA, ILEANA | 1633 | 435-320100 |

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a **Customer Number is required.**

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 _____
 (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 _____
 3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee
☐ Publication Fee (No small entity discount permitted)
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4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.
☐ Payment by credit card. Form PTO-2038 is attached.
☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. Change in Entity Status (from status indicated above)

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

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This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 58 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 58 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Notice of Allowability**Application No.**

10/500,173

Applicant(s)

TAKAHASHI ET AL.

Examiner

ILEANA POPA

Art Unit

1633

- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the applicant reply filed on 01/19/2010.
2. ☒ The allowed claim(s) is/are 1,6,7,25,26 and 35-39.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☒ Some* c) ☐ None of the:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: English language translation of the foreign priority documents.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
(a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
(b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413),
Paper No./Mail Date _____
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____

/Ileana Popa/
Primary Examiner, Art Unit 1633

EXAMINER'S AMENDMENT

1. The instant claims are allowable subject to the amendments below.
2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Serge Ilin-Schneider on 4/23/2010.

The application has been amended as follows:

Claims 20 and 21 are cancelled.

Claim 1 is rewritten as follows:

--**"A herpes simplex virus vector (HSV vector) that does not replicate in adult normal cells, but specifically replicates and is expressed in proliferating cells expressing calponin, and that is capable of suppressing its replication at a desired time by using the thymidine kinase gene, wherein the HSV vector is a recombinant HSV vector with a DNA fragment comprising:**

(i) the promoter region of the human calponin gene consisting of the nucleotide sequence of SEQ ID NO.: 3;

(ii) an ICP4 gene encoding a transcription factor essential for initiation of a herpes viral replication operably linked downstream the promoter region of the human calponin gene,

(iii) an EGFP gene operably linked downstream the ICP4 gene via an internal ribosomal entry site; and

(iv) a LacZ gene integrated upstream to the said promoter region of the human calponin gene;

wherein the DNA fragment is inserted by homologous recombination into the ribonucleotide reductase gene locus of an HSV vector that comprises an endogenous thymidine kinase gene and lacks functional endogenous ICP4 gene, and wherein the expression of both the LacZ gene and the EGFP gene is used to identify the recombinant HSV vector.”

Claim 6 is rewritten as follows:

--“The HSV vector according to claim 1, wherein an enhancer is operably linked upstream to the promoter region of the human calponin gene.”

Claim 25 is rewritten as follows:

--“The method according to any one of claims 37 or 38, wherein the cells and tissues in the organism are tumor tissues, vascular or lymphatic vessel constriction tissues, nephritic tissues or fibrotic tissues.”

Claim 26 is rewritten as follows:

--**"A therapeutic composition comprising the HSV vector according to claim 1 wherein the proliferating cells are smooth muscle cells."**

Claim 35 is rewritten as follows:

--**"A method for producing a cell-specific recombinant HSV vector that does not replicate in adult normal cells, but replicates and is expressed specifically in a proliferating cells that express calponin, and that is capable of suppressing its replication at a desired time by using the thymidine kinase gene, said method comprising the steps of:**

(a) preparing a DNA fragment comprising,

(i) the promoter region of the human calponin gene consisting of the nucleotide sequence of SEQ ID NO.: 3,

(ii) an ICP4 gene encoding a transcription factor essential for initiation of HSV replication operably linked downstream the promoter region of the human calponin gene,

(iii) an EGFP gene operably linked downstream the ICP4 gene via an internal ribosomal entry site, and

(iv) a LacZ gene integrated upstream the promoter region of the human calponin gene,

(b) cotransfecting the DNA fragment with an HSV vector that comprises an endogenous thymidine kinase gene and lacks functional endogenous ICP4 gene

into a cell in which the promoter region of the human calponin gene consisting of the nucleotide sequence of SEQ ID NO.: 3 can be activated; wherein the DNA fragment is inserted by homologous recombination into the ribonucleotide reductase gene locus of the HSV vector to produce HSV recombinant vectors, and

(c) selecting a single clone of recombinant HSV vector expressing both LacZ and EGFP genes via screening the HSV recombinant vectors by limiting dilution without agarose overlay assay using both the LacZ gene and the EGFP gene as markers.”

Introduce new claims 37-39.

Claim 37 is written as follows:

--“The recombinant HSV vector of claim 1, further comprising a heterologous gene encoding a protein or a peptide of interest.”

Claim 38 is written as follows:

--“A method for expressing a gene, protein or a peptide comprising introducing the HSV vector according to claim 37 into the cells and tissues of an organism, then expressing the gene, protein, or peptide of the vector.”

Claim 39 is written as follows:

--“A method for suppressing the expression of a gene, protein or a peptide of the HSV vector according to claim 37 comprising,

(i) introducing the HSV vector according to claim 37 into the cells and tissues of an organism,

(ii) expressing the gene, protein or peptide of the vector, and

(iii) suppressing the expression of the gene, protein or peptide at a later desired time by administering an antiviral drug, wherein said antiviral drug is aciclovir or ganciclovir.”

3. **The disclosure is amended as follows:**

Page 33, line 12 replace “dl2.cndot.CALP.cndot..ARR” with “d12-CALP-ΔRR”

4. The following is the examiner's statement of allowance:

The claimed invention is drawn to a specific HSV vector, wherein the HSV vector comprises the calponin promoter set forth by SEQ ID NO: 3. It is noted that SEQ ID NO: 3 is free of the prior art of record. The claimed vector is capable of being expressed in malignant cells without affecting the normal cells. Therefore, the claimed invention as amended *supra* is allowable.

Any comments considered necessary by the applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled “Comments on Statement of Reasons for Allowance.”

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Primary Examiner, Art Unit 1633